L2 and S2. The coordinates are in relation to a Cartesian set of orthogonal axes. The L1, S1 and L2 domains of the EGF receptor models have been superimposed on the crystal structure of the IGF-1 receptor domains L1, cysteine-rich domain and L2. The final column contains the number 20, 40 or 60, depending on whether the residue containing the atom is judged to be well-modeled, have a moderate possibility of error, or is likely to be inaccurate, respectively. --

A1

IN THE CLAIMS:

Please amend claims 1-13, 15 and 17-23 and add new claims 54-56 as follows:

A2

Claim 1 (Amended). A method of designing or selecting a compound which binds to a molecule of the EGF receptor family and modulates an activity mediated by the molecule, which method comprises

Amend. D1

(A) assessing the stereochemical complementarity between the compound and a topographic region of the molecule, wherein the molecule comprises

(i) amino acids 1-621 of the EGF receptor positioned at atomic coordinates substantially as shown in Figure 6;

(ii) one or more subsets of said amino acids related to the coordinates shown in Figure 6 by whole body translations and/or rotations;

(iii) amino acids present in the amino acid sequence of a member of the EGF receptor family, which form an equivalent three-dimensional structure to that of the receptor site defined by amino acids 1-621 of the EGF receptor positioned at atomic coordinates substantially as shown in Figure 6;

(B) obtaining a compound which possesses stereochemical complementarity to a topographic region of the molecule; and

(C) testing the compound for its ability to modulate an activity mediated by the molecule.

Claim 2 (Amended). A method as claimed in claim 1 in which the compound is selected to complement the topographic region of the molecule is defined by amino acids 1-475 of the EGF receptor positioned at atomic coordinates substantially as shown in Figure 6, or an amino acid sequence which forms an equivalent three-dimensional structure to that of the region defined by amino acids 1-475 of the EGF receptor positioned at atomic coordinates substantially as shown in Figure 6.

D

Claim 3 (Amended). A method as claimed in claim 1 in which the compound is selected to complement the topographic region of the molecule is defined by amino acids 313-621 of the EGF receptor positioned at atomic coordinates substantially as shown in Figure 6, or an amino acid sequence which forms an equivalent three-dimensional structure to that of the region defined by amino acids 313-621 of the EGF receptor positioned at atomic coordinates substantially as shown in Figure 6.

A2

Claim 4 (Twice Amended). A method as claimed in claim 1 in which the compound is designed or selected so as to complement the structure of a topographic region of the molecule as depicted in Figure 5.

Claim 5 (Twice Amended). A method as claimed in claim 1 in which the compound is designed or selected to comprise structural regions able to make close contact with amino acid residues at the surface of the molecule lining a groove region as depicted in Figure 7, Figure 8 or Figure 9.

Claim 6 (Twice Amended). A method as claimed in claim 1, in which the compound is designed or selected to have a stereochemistry such that it can interact with both the L1 and L2 domains of the molecule.

D

Claim 7 (Twice Amended). A method as claimed in claim 1, in which the compound is designed or selected to interact with the region of the L1 domain-S1 domain interface, causing an alteration in the positions of the L1 and S1 domains relative to each other.

Claim 8 (Twice Amended). A method as claimed in claim 1, in which the compound is designed or selected to interact with a hinge region between the L2 domain and the S1 domain causing an alteration in the positions of the L2 and S1 domains relative to each other.

subC1 Claim 9 (Twice Amended). A method as claimed in claim 1, in which the compound is designed or selected to interact with the -sheet of the L1 domain causing an alteration in the position of the L1 domain relative to the position of the S1 domain or the L2 domain.

Claim 10 (Twice Amended). A method as claimed in claim 1, in which the compound is designed or selected to have a stereochemistry such that it can interact with both the L2 and S2 domains of the molecule.

Claim 11 (Twice Amended). A method as claimed in claim 1, in which the compound is designed or selected to interact with a hinge region between the L2 domain and the S2 domains causing an alteration in the positions of the L2 and S2 domains relative to each other.

Claim 12 (Twice Amended). A method as claimed in claim 1, in which the compound is designed or selected to interact with the -sheet of the L2 domain causing an alteration in the position of the L2 domain relative to the position of the S2 domain.

Claim 13 (Twice Amended). A method as claimed in claim 1 in which the compound is designed or selected to bind to a lower face containing the second -sheet of the L1 and/or L2 domains, wherein the structure of the face is characterized by a plurality of solvent-exposed hydrophobic residues.

Claim 15 (Twice Amended). A method as claimed in claim 1, in which the compound is designed or selected to have a stereo complementarity with the receptor site of the molecule such that the compound has a K_d for the receptor site of less than 10^{-6} M.

Claim 17 (Twice Amended). A method as claimed in claim 1 in which the compound is designed or selected from or modified from test compounds identified from a data base.

Claim 18 (Twice Amended). A method according to claim 1, in which the compound is designed or selected to have the ability to increase an activity mediated by a molecule of the EGF receptor family.

Claim 19 (Twice Amended). A method according to claim 1, in which the compound is designed or selected to have the ability to decrease an activity mediated by a molecule of the EGF receptor family.

Claim 20 (Amended). A method according to claim 19, in which the molecule is designed or selected to have a stereochemical interaction with the compound and the molecule that prevents the binding of a natural ligand of the receptor molecule to the receptor site.

Claim 21 (Twice Amended). A method according to claim 19, in which the compound designed or selected to have a K_1 of less than 10^{-6} M.

Claim 22 (Amended). A method according to claim 19, in which the compound is designed or selected to have a K_1 of less than 10^{-8} M.